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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/066,305	01/31/2002	Todd R. Golub	2825.2023-001	2026

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No.	Applicant(s)	
	10/066,305	GOLUB ET AL.	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,16,19,20,23-29,31 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,16,19,20,23-29,31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-13 have been canceled. Claims 35-41 have been added. Claims 14, 16, 19, 20, 23-29, 31 and 32 have been amended. Claims 14, 16-20, 23-29, 31, 32 and 35-41 are pending and under consideration.

2. The text of title 35, U.S. code not cited in this action can be found in a previous action.

3. Claims 31 and 32 are objected to because of the following informalities: medulloblastoma is misspelled. Appropriate correction is required.

4. Claims 24, 25, 28, 29, 40 and 41 are objected to for being drawn to non-elected inventions.

5. Claims 14, 16-20, 23-29, 31, 32 and 35-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

(A) Claims 26 has been amended to recite the limitation "wherein class distinction is made with reference to a first or second class, wherein the first class is good prognosis of survival after treatment and the second class is a prognosis of treatment failure. The specification as filed fails to provide support for this amendment.

(B) Claims 14, 26, 31, and 32 recite nucleotides 3336-3720 of GenBank Accession Number M64347. There is no support in the specification for the specific limitations of nucleotides 3336-3720 of GenBank Accession Number M64347.

6. The rejection of Claims 14, 16-20, 23-29, 31, 32 and 35-41 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained for reasons of record. New claims 35-41 are also rejected for the same reasons of record..

The claims are rendered vague and indefinite in the recitation of residues of a GenBank Accession number at as the only means for identifying the claimed informative gene. Applicant argues that one of skill in the art would know if the sequence had been modified. This is not persuasive. The M.P.E.P. states that there are two requirements under 112, 2nd paragraph

(A) the claims must set forth the subject matter that applicants regard as their invention;

and

(B) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant.

Regarding part B, if the sequence of the GenBank Accession Number was altered in the future, the metes and bonds of the subject matter that would be protected by the patent would not be clear.

Applicant further argues that the PTO has granted some 18 patents with claims drawn to GenBank Accession Numbers. This argument is irrelevant. Only the instant application is being examined at this time.

Claims 19 and 20 lack active method steps, as the recitation of "utilizing" does not constitute a specific method step.

Claim 23 is vague and indefinite in the recitation of "survival after treatment" without limitations as to how long said survival shall occur. Survival after treatment can encompass a length of time as small as an hour or a week, or a length of time such as 5 years, or 10 years.

Claim 26 is vague and indefinite in the recitation of "informative genes" . further it is unclear how the "magnitude" of the vote is to be determined because "depending on the expression level of the gene" does not accurately define the mathematical relationship between the gene expression and the magnitude of the vote; further, the relationship between the gene expression and class distinction is unclear. this lack of clarity stems from a lack of a definition for "class distinction" . Additionally, the claims are vague and indefinite because it is unclear if the level of gene expression used in the computation is a normalized or non-normalized level. Section (b) of claim 26 is vague and indefinite because "winning " would be a relative term. The specification nor claim provides a level at which the summation of votes is either "winning" or

"loosing". Claim 26 is vague and indefinite in the recitation of "summing the votes" as referred to in the plural as it appears from section (a) that one informative gene is given a single weighted vote. It is unclear how a single weighted vote from one gene is to be subjected to "summing". The claim also fails to link by an active method step the summation of the votes to the determination of "the winning class" and further fails to link by an active method step said "winning class" with a treatment outcome class.

The metes and bound of claim 27 cannot be determined. Claim 27 fails to recite how a correlation is made between gene expression values and class distinction. It is unclear how a log10 gene expression value differs from the log10 gene expression level in the sample to be tested rendering the value of xg vague and indefinite. In addition, claim 27 recites "in the sample to be tested" in reference to the xg value. However, neither of claims 26 or 27 are drawn to a sample to be tested; they are drawn to a method of assigning a brain tumor sample to a treatment outcome class. Therefore, the reference to "gene expression value in the sample to be tested" is vague and indefinite as the sample would already have been tested for gene expression in order to determine the weighted vote for claim 26. Additionally, the claims are vague and indefinite because it is unclear if the level of gene expression used in the computation is a normalized or non-normalized level. It is unclear how a vote for the "first class" versus a vote for the "second class" in claim 27 effects the prediction of treatment outcome which is the method objective recited in claim 26.

Applicant argues that informative genes are those which correlate with treatment outcome. However this does not satisfy the requirements of 112, 2nd paragraph because the informative genes must necessarily be defined by the specification in order to establish the metes and bounds of the claims.

Applicant argues that the claims have been amended to clarify the distinction between the first and the second class. This is true, however, the amendment constitutes new matter for the reasons set forth above. When the new matter is canceled the rejection under 112, 2nd will be reapplied.

Applicant argues that it is irrelevant if the level of gene expression if normalized or non-normalized because one of skill in the art would know whether the gene expression levels should be normalized or not. This has been considered but not found persuasive. The metes and bounds

of the claims would change substantially based on what would be used as the normalizing value. Thus the limit of the claims cannot be construed.

Applicant argues that the specification teaches what constitutes treatment success or failure in terms of disease free survival or length of survival because the specification state "patients who are alive following treatment compared to patients who succumbed to their disease". This is not persuasive. Alive following treatment can be interpreted as 1 hour after treatment, six months after treatment, five years after treatment. For this reasons, alive following treatment and succumbing to their disease are both open-ended.

Applicant argues that methods of defining classes and classifying samples are described in US 6,647,341. However, being able to define classes and classifying samples by the method of Golub et al does not provide the metes and bounds of the parameters in question for the instant claims. Applicant seems to be confusing the requirements of 112, first paragraph for the requirements of 112, 2nd paragraph.

7. Claims 40 and 41 contains the trademark/trade name Affymetrix HuGeneFL array. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe the probes in the array and, accordingly, the identification/description is indefinite.

8. The rejection of claims 14, 16-20 and 23-25 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn in light of applicants amendment. However, applicant's

amendment constitutes new matter. In the event that the new mater is canceled, the rejection will be re-applied and applied to new claims 35-41 as well.

9. The rejection of claims 31 and 32 under 35 U.S.C. 103(a) as being unpatentable over Au-Young et al (U.S. 6,500,938, cited in a previous Office action) in view of Abbass et al (Journal of Clinical Endocrinology and Metabolism, 1997, Vol. 82, pp. 1160-1166, cited in a previous Office action) is withdrawn in light of applicant amendment which excludes the pituitary adenoma. .

10. The rejection of claims 31 and 32 under 35 U.S.C. 103(a) as being unpatentable over Friend et al (U.S. 6,218,122, cited in a previous Office action) in view of Abbass et al (Journal of Clinical Endocrinology and Metabolism, 1997, Vol. 82, pp. 1160-1166) is withdrawn in light of applicant amendment which excludes pituitary adenoma.

11. All other rejections and objections as set forth in the previous Office action are withdrawn.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571)272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
10/4/2004

Karen A. Canella

KAREN A. CANELLA PH.D
PRIMARY EXAMINER